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Institutionen för Biovetenskaper och Näringslära

Characterization of evolutionary conserved subdivisions in the embryonic zebrafish forebrain based on gene expression patterns

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ABSTRACT

Intersecting transverse and longitudinal transcription factor expression domains divide the embryonic brain into a grid of histogenetic fields with distinct positional identities. The topology of histogenetic fields has been highly conserved during vertebrate evolution and can therefore be used to reveal homologous relations of brain areas between vertebrates. In order to further establish zebrafish as a model system to study vertebrate brain development and related neurological disorders, homologous relationships of zebrafish and mammalian brain regions have to be clarified. For this purpose we developed a multi-color fluorescent in situ hybridization (FISH) protocol to distinguish abutting and overlapping gene expression patterns at high-resolution. We improved the sensitivity of peroxidase (POD) based FISH through the inclusion of the polymer dextran sulfate into hybridization and substrate reaction and the application of substituted phenol compounds as POD accelerators. The utilization of bench-made fluorogenic POD substrates further increased sensitivity and allowed for detection of up to three different transcripts simultaneously. This multi-color FISH method was used to generate a comprehensive map of regulatory gene expression domains of the embryonic zebrafish diencephalon and hypothalamus. Our analysis was consistent with a three prosomeric organization of the zebrafish diencephalon. It also showed that intraprosomeric subdomains in the alar pretectum, thalamus and prethalamus have been conserved. The strikingly similar topology of hypothalamic gene expression domains of murine and fish orthologues transcription factors allowed identifying homologous progenitor domains. Using corticotropin-releasing hormone as a molecular differentiation marker we could further establish homology between the nucleus preopticus and the paraventricular nucleus as well as for the suprammillary band in fish and mammals. The detailed expression maps determined in this work also provides a predictive tool to aid functional studies on genetic pathways involved in specification of neuronal fields and cell types. The compilation of embryological zebrafish expression data in gene maps will facilitate comparisons across species and help to promote studies on vertebrate brain development and neurological disorders using zebrafish.

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